REMARKS

Claims 1 to 35, 38 to 40, and 71 to 113 are in the application. Claims 1, 25, 31 to 35, 38, 71 to 74 and 98 have been amended. Claim 1 has been amended to include the term "the wall of". Claims 112 and 113 have been added which describe the thickness of the shell wall. Claims 31 to 35, 71 to 74 and 98 have been amended to remove the tradename Eudragit 4135 as well as to correct for various typographical errors, etc. Support for these amendments and newly added claims lie in the specification on page 4, lines 13 to 15 and page 5, lines 29 to 33. No new matter is believed added.

Claims Objections

Claims 31, 35 and 72 have been objected to as containing multiple periods after the example numbers. Claims 31, 35, 71 and 72 have been amended to remove this objection.

Claims 31 to 35, 71 and 72 are objected to as being unclear whether each embodiment listed individually in the claims is intended to be in the alternative. Applicants respectfully traverse this objection.

The presentation of the formulations contained in these claims is not believed to be new nor an unusual way of presenting these formulations. These claims are believed to be clear and concise as to what each formulation contains, regardless of whether they are independent or dependent. Each formulation was labeled with an example number which clearly indicates that each is independent from the next one, although it is not believed that this column is even needed. In one instance, Claim 71 the word "or" was present to indicate that they are independent from each other. The claim has been amended however to remove this term and to make all of the formulation specific claims consistent.

Rejection of Claims under 35 USC §112

Claim 31 is rejected under 35 USC §112, 2nd paragraph as being indefinite. Claim 31, containing examples 14 and 15 both contain errors in that their amounts do not add up to 100% but 95 and 105 % w/w respectively. Claim 31 has been amended to delete both formulations. The Example # column has also been deleted.

In view of these amendments, withdrawal of the rejection to the claim is respectfully requested.

Rejection of Claims under 35 USC §103

Claims 1 to 35, 38 to 41 and 71 to 111 are rejected under 35 U.S.C. § 103(a) as being obvious over Hatano et al. US Patent No. 6,309,666 ('666) in view of Lehmann et al. US Patent No. 5,705,189 ('189), hereinafter Lehmann I, and Lehmann et al. (US Patent No. 5,644,011 ('011), hereinafter Lehmann II. Applicants respectfully traverse this rejection.

As noted previously the claims have been amended to more clearly define the invention as a capsule, a linker or subunit which is itself composed of the composition as claimed therein.

The composition and articles thereof are clearly in direct contrast to the teachings of Hatano which produce a "coated capsule compositions comprising a hard outer shell (See Abstract)". The Examiner recognizes that the "Hatano et al. patent does not disclose a molding process for making the disclosed hard outer capsule shells, nor does it disclose the use of a copolymer of methyl acrylate, methyl methacrylate, and methacrylic acid in a ratio of 7:3:1." *See* Office Action, page 4, ¶2.

Hatano does not disclose or suggest a molding process for making capsule shell components. Hatano is interested in using pre-existing capsule shells and coating these shells to have particular release features. Hatano does not disclose or suggest capsule linker or subunits as covered by claims 73 to 111.

To summarize Applicants previous response, the Hatano et al. patent discloses a pulse release dosage form performance having the following characteristics:

1. An Enteric layer (acrylic copolymer) that dissolves when the unit enters the small intestine and is exposed to pH>5.5
2. An inner layer of E100 polymer swells and hydrates but does not dissolve
3. Fluid enters the capsule body (dissolving the gelatin of HPMC capsule wall) at a rate determined by the thickness of the E100 coating and begins to dissolve the acidic capsule contents, and

4. Dissolution of the E100 layer is controlled by the amount and/or type of acid contained within the capsule fill and the thickness of the E100 coating.

The Examiner has now cited two Lehmann et al. patents as secondary references to support the failure of Hatano to disclose molding of capsule shells. In the Interview of December 2005, the Lehman I patent (as well as the Hatano et al. patent) were discussed in detail and overcome, it was believed, by the failure of Hatano to direct the skilled artisan to look elsewhere at a secondary reference and achieve the claimed subject matter of the composition being the actual shell wall or the linker/subunits (as presented in Applicants amended claims in the January response).

The Lehman II patent does not provide any additional support for that which is already missing in the Hatano or Lehmann I patent to direct the skilled artisan to make the necessary modifications to Hatano et al and achieve applicants claimed subject matter.

The Lehman II patent, US 5,644,011 relates to compositions of polymers and their emulsion for use as coating agents (in this instance FS30D, the dispersed form of 4135F). These coating emulsions are used to achieve an enteric seal coat which dissolves at pH>6.5. Specifically, the emulsions are applied as film-coating agents to achieve a pH-dependent release between pH 6-7.5.

Column 4 lines 23-33 of Lehmann II indicate that these polymers are suitable for melt-processing (viscosity data and thermal stability/TGA data supplied), but the patent does not describe, nor suggest that there is a formulation taught therein which is suitable for injection molding. The mere suggestion that a polymer can be melted does not mean that it can be injection molded, nor that it can be made into capsule shells, etc. which have particular dimensional requirements, e.g. wall thickness, etc. such as those claimed in newly added claims 112 and 113.

For commercial usage, it is desired that the wall thickness of the capsule shell be generally uniform, and in the range of about 0.3 mm to 0.5 mm. in order to achieve adequate strength, allowing the capsule shells to be formed and handled without

breakage or distortion. In addition, an injection-moulded capsule shell has a significantly increased thickness as compared to a gelatin capsule containing a film-coated layer.

It appears that the Examiner does not understand the differences between film-coating with an acrylic copolymer to achieve an enteric capsule (both exemplified in Hatano and Lehmann patent II) and the use of an acrylic copolymer in combination with particular excipients (such as the dissolution modifying excipients as claimed herein) to achieve a pulsatile release which is pH-independent and depends not on a multi-layer construct as described by Hatano but on the polymeric composition of a single layer. Lehmann II teaches that these polymeric compositions are pH dependent. Clearly, in Column 2, lines 61 to 65 that is the result desired. There is no recognition that the polymeric compositions described therein can be modified to produce such a result.

The present formulations as claimed (and amended) comprise the wall of a capsule shell and are produced by an injection molding process (the subject of a divisional application). These capsule formulations achieve a dissolution profile which is not completely acid dependent, a surprising result from that taught in the art, and also possess suitable tensile characteristics to allow for automated filling and assembly. Neither the Hatano and Lehmann I or II references teach these compositions, nor these results. The Lehmann patent I does not direct the reader to compositions with suitable mechanical properties for commercialization as a capsule dosage form as discussed in Applicants earlier responses which are incorporated herein by reference. This failure is not remedied by the Lehmann II patent which does not provide any motivation to achieve a formulation suitable for capsule shell molding.

The present invention requires (Claim 1) the addition of a dissolution modifying excipient (DME) present in amounts of 2.5 to 70% by weight. DME's are described in Applicants specification on page 27, lines 25 to 35 and page 28, lines 1 to 34. Specifically, claims 11 to 13 require the DME to be a swellable solid, such as HPMC, or HPC.

Claims 14 and 15 require the DME to be a non-reducing sugar, a water soluble filler or a disintegrant. Claims 16 and 17 are directed to various combinations of the DME agents, e.g. a swellable solid and a non-reducing sugar, a water soluble filler or a disintegrant. Lehman I does not disclose the use of a DME in their compositions. Lehman I does not disclose nor suggest a combination of DME agents.

Lehmann I also does not disclose the use of stearyl alcohol, talc, magnesium stearate, silicon dioxide, amorphous silicic acid, or fumed silica or combinations thereof as alternative lubricants. Claims 9 and 10 specifically require the use of stearyl alcohol.

The Lehmann I patent also does not disclose the use of surfactants, as disclosed in Applicants specification on page 26, lines 15 to 37, and page 27, lines 1 to 3, and as claimed in Claims 3, 4, 5, 6, and 18 to 21.

While Applicant has included as a DME a "super disintegrant", such as croscarmellose sodium, copovidone, or sodium starch glycollate (Claims 14, and 16). These superdisintegrants are typically utilized in the pharmaceutical industry for compressed tablet formulations (to aid in dissolution), not in the structural wall of a capsule shell. Lehman I does not disclose use of a super disintegrant.

The Lehmann II patent also does not teach incorporation of these specific excipients, nor in the particular amounts as claimed herein.

There is no motivation present in either of the Lehmann et al. patents to direct the skilled artisan to include these excipients, specifically the DME's, let alone a disintegrant, etc. in a composition suitable for molding capsule shells, linkers and subunits.

As previously stated, Hatano et al. does <u>not</u> direct the skilled artisan to utilize a thermoplastic polymer to mold capsule shells. Hatano et al. would not look to the disclosure of Lehman et al. to achieve these characteristics. As a result, the Office has failed to make out a *prima facie* case of obviousness.

In looking at the requirements for maintaining a *prima facie* case of obviousness, one is the reasonable expectation of success. The Office has provided no basis for this

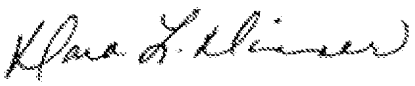
requirement. Lehman I which does discuss the need for a plasticizer and a mold-releasing agent, does not provide any values for the recited concentrations of any additional excipients, i.e. stearyl alcohol, dissolution modifying excipients, and superdisintegrants, which appear in Applicants specification and claims. As shown in the Interview, the polymer 4135 is basically not moldable without the inclusion of Applicants additional agents. It has long been settled that for obviousness purposes, the reasonable expectation of success must not come from the applicant's own disclosures, and consequently these two references in combination fail to provide a reasonable expectation of success.

In view of the Interview, remarks, and amendments herein, it is believed that there is no longer the necessity for a showing of unexpected results to obviate the obviousness rejection. Because there is no *prima facie* case of obviousness in view of Hatano et al., taken with Lehman et al., Applicants do not bear the burden of making such a showing at this juncture. Having established that the Office has failed to set forth a *prima facie* case of obviousness, Applicants respectfully request the withdrawal of the §103 rejection to the claims and issuance of a Notice of Allowance.

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. It is not believed that this paper should cause any additional fees or charges to be required, other than expressly provided for already. However, if this is not the case the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Date: July 19, 2006

Respectfully submitted,



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